Appl. No. 10/052,589

Amdt. dated: November 9, 2004

Reply to Office Action of May 19, 2004

## Amendments to the Specification:

Please amend the figure description beginning on page 3, line 19 as follows:

Figure 2 is the DNA sequence, SEQ ID NO. 3, of the promoter of the murine  $\alpha_{1B}$  adrenergic receptor.

Please amend the figure description beginning on line 22 of page 3, as follows:

Figure 4. (A) A map of the transgene construct showing the size of EcoRI fragments and the binding sites for  $\alpha_{1B}$  - and SV40-specific southern probes. Three different transgenes were constructed with the only difference between each being the  $\alpha_{1B}AR$  cDNA used (either the wildtype (WT), single mutant or triple mutant cDNA). Transgenic animals whose genome contain the wild-type transgene are designated W; transgenic animals whose genome contain the single mutant transgene are designated S; and transgenic animals whose genome contain the triple mutant transgene are designated T. Each founder transgenic animal and its progeny are also given a numerical designation. For example, one of the founder transgenic animals whose genome contains the wild-type transgene, and its progeny, is referred to as "W1", while another transgenic founder animal whose genome contains the wild-type transgene, and its progeny, is referred to as "W2". (B) Southern blot analysis of genomic DNA from nontransgenic (NT)(-/-), heterozygous (+/-) and homozygous (+/+) W2 mice. Tail DNA samples were digested with EcoRI, run on 0.8% agarose gels, transferred to nitrocellulose and probed with either the  $\alpha_{1B}$ probe or the SV40 probe. The  $\alpha_{1B}$  probe hybridized to 3.0 and 1.6 kb fragments which represented the endogenous  $\alpha_{1B}AR$  gene and the transgene respectively. Comparatively, the SV40 probe hybridized only to a 1.4 kb fragment which represented the transgene. (C)  $B_{max}$ determination was carried out via saturation binding in various  $\alpha_{1B}AR$  -positive and -negative tissues using the  $\alpha_1$ -antagonist 2-[ $\beta$ -(4-hydroxyl-3-[ $^{125}$ I]iodophenyl)ethylaminomethyl]tetralone ([ $^{125}$ I]HEAT) as the radioligand.  $B_{max}$  values in W2+/- mice that were significantly different from the corresponding non-transgenic (NT) values are labeled with an asterisk. Error bars represent SEM (N>5 for each tissue) and significance was determined using analysis of variance with a two-tailed Student's t test (p<0.05). (D) Inositol tri-phosphate (IP<sub>3</sub>)levels. Error bars represent SEM (n=3 for each line) and significance was determined using analysis of variance with a two-tailed Student's t test (p<0.05). The asterisk (\*) indicates significance from the NT

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group. The dagger (†) indicates significant increases compared to the W2+/- group. The double cross (‡) indicates significant increases compared to the S l+/- group.. (E) Hybridization pattern of the SV40 probe in a section cut from a NT mouse. (F) Hybridization pattern of the  $\alpha_{1B}$  probe to endogenously expressed  $\alpha_{1B}AR$  transcripts in a NT brain section. (G) Hybridization of the SV40 probe to message transcribed from the transgene in the brain of a W2+/- mouse. Cx = cortex; Rt = reticular thalamic nuclei; Hy = hypothalamus. (H) Transgene expression detected by the alB probe. These positive regions coincide with regions identified in C and overlap the background expression of the endogenous gene.